

His Ser Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
1 5 10 15
Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30
Ser Gly Ala Pro Pro Pro Ser-NH₂
35

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100

FIGURE 1

EXENDIN-4

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
5 10 15
Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30
Ser Gly Ala Pro Pro Pro Ser-NH₂
35

EXENDIN-4

FIGURE 2

6 / 11

GLP-1 (GLP-1(7-36)NH₂)

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg-NH₂
 20 25 30

FIGURE 3

Page 1

Figure 4

Page 2

Figure 4

Figure 4

Amino Acid Position	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39
Compound 72	Ala	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Ala	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	Pro	NH2		
Compound 73	Ala	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 74	His	Gly	Ala	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 75	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 76	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 77	Ala	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 78	His	Gly	Ala	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 79	His	Gly	Glu	Ala	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 80	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 81	Ala	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 82	His	Gly	Ala	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 83	His	Gly	Glu	Ala	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	Pro	Pro	NH2	
Compound 84	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	Pro	Pro	NH2	
Compound 85	Ala	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Ala	Nme	NH2		
Compound 86	His	Gly	Ala	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	Pro	NH2	
Compound 87	His	Gly	Asp	Ala	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	NH2			
Compound 88	Ala	Gly	Gly	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	Pro	Pro	NH2
Compound 89	Ala	Gly	Ala	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	Gly	Gly	Pro	Ser	Ser	Gly	Gly	Ala	Pro	Pro	NH2

Glucose lowering effect in db/db mice at 1 hr time point

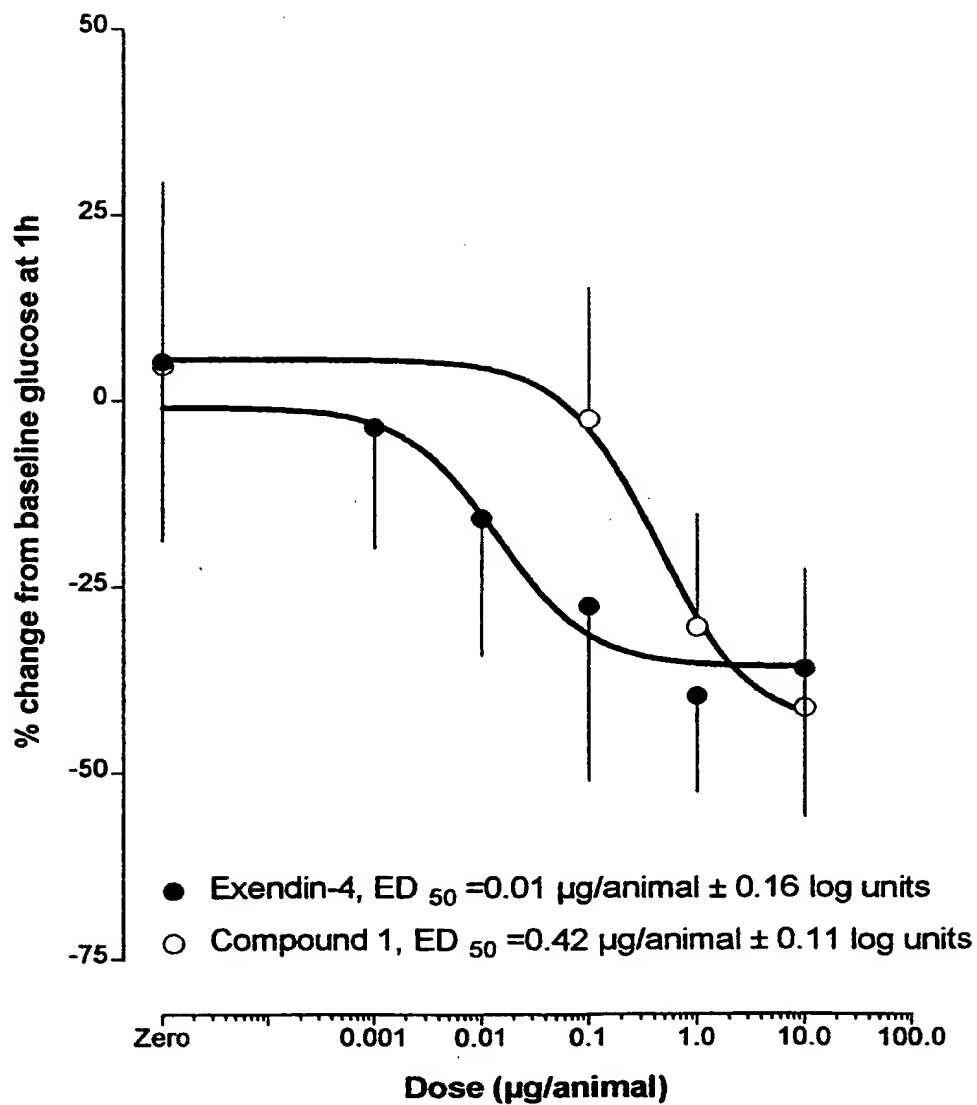


Figure 5

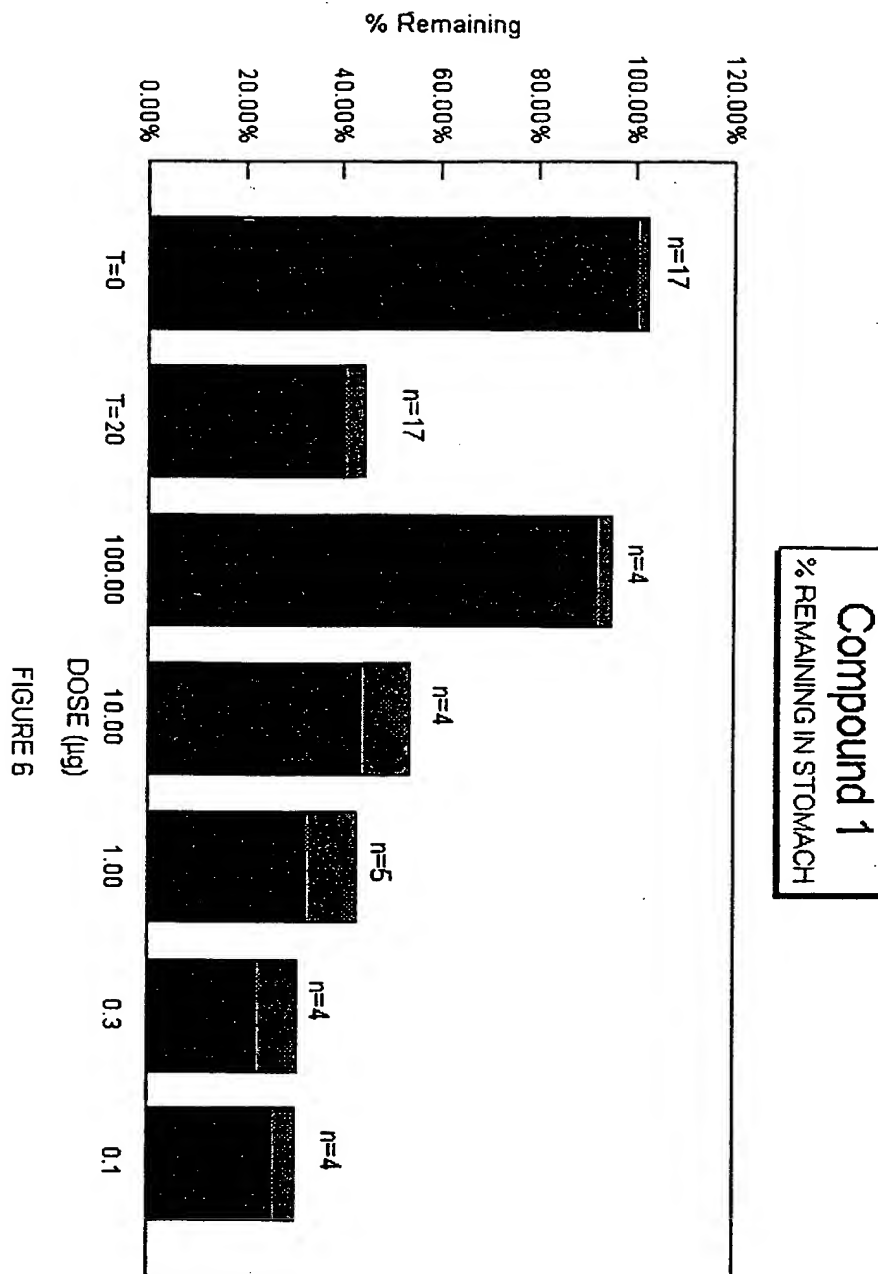


FIGURE 6

FIGURE 7

Cmp
No.

- 90 4-Imidazolypropionyl-Gly Glu Gly Thr Phe Thr Ser Ala Leu
Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp
Leu Lys-NH^εoctanoyl Asn-NH₂ [SEQ. ID. NO. 95]
- 91 4-Imidazolypropionyl-Gly Glu Gly Thr Phe Thr Ser Ala Leu
Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe
Leu Lys-NH^εoctanoyl Asn-NH₂ [SEQ. ID. NO. 96]
- 92 4-Imidazolypropionyl-Gly Glu Gly Thr Phe Thr Ser Ala Leu
Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp
Leu Lys-NH^εoctanoyl Asn Gly Gly-NH₂ [SEQ. ID. NO. 97]
- 93 4-Imidazolypropionyl-Gly Glu Gly Thr Phe Thr Ser Ala Leu
Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe
Leu Lys-NH^εoctanoyl Asn Gly Gly-NH₂ [SEQ. ID. NO. 98]
- 94 4-Imidazolypropionyl-Gly Glu Gly Thr Phe Thr Ser Ala Leu
Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp
Leu Asn Lys-NH^εoctanoyl-NH₂ [SEQ. ID. NO. 99]
- 95 4-Imidazolypropionyl-Gly Glu Gly Thr Phe Thr Ser Ala Leu
Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe
Leu Asn Lys-NH^εoctanoyl-NH₂ [SEQ. ID. NO. 100]

- 96 4-Imidazolypropionyl-Gly Glu Gly Thr Phe Thr Ser Ala Leu
Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp
Leu Asn Lys-NH^coctanoyl Gly Gly-NH₂ [SEQ. ID. NO. 101]
- 97 4-Imidazolypropionyl-Gly Glu Gly Thr Phe Thr Ser Ala Leu
Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe
Leu Asn Lys-NH^coctanoyl Gly Gly-NH₂ [SEQ. ID. NO. 102]
- 98 Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu
Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys-NH^coctanoyl
Asn-NH₂ [SEQ. ID. NO. 103]
- 99 Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu
Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys-NH^coctanoyl
Asn-NH₂ [SEQ. ID. NO. 104]
- 100 Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu
Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys-NH^coctanoyl
Asn Gly Gly-NH₂ [SEQ. ID. NO. 105]
- 101 Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu
Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys-NH^coctanoyl
Asn Gly Gly-NH₂ [SEQ. ID. NO. 106]
- 102 Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu
Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Asn Lys-
NH^coctanoyl-NH₂ [SEQ. ID. NO. 107]

3 / 11

103 Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu
Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Asn Lys-
NH^εoctanoyl-NH₂ [SEQ. ID. NO. 108]

104 Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu
Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Asn Lys-
NH^εoctanoyl Gly Gly-NH₂ [SEQ. ID. NO. 109]

105 Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu
Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Asn Lys-
NH^εoctanoyl Gly Gly-NH₂ [SEQ. ID. NO. 110]